# The dark side of our genes – healthy aging in modern times

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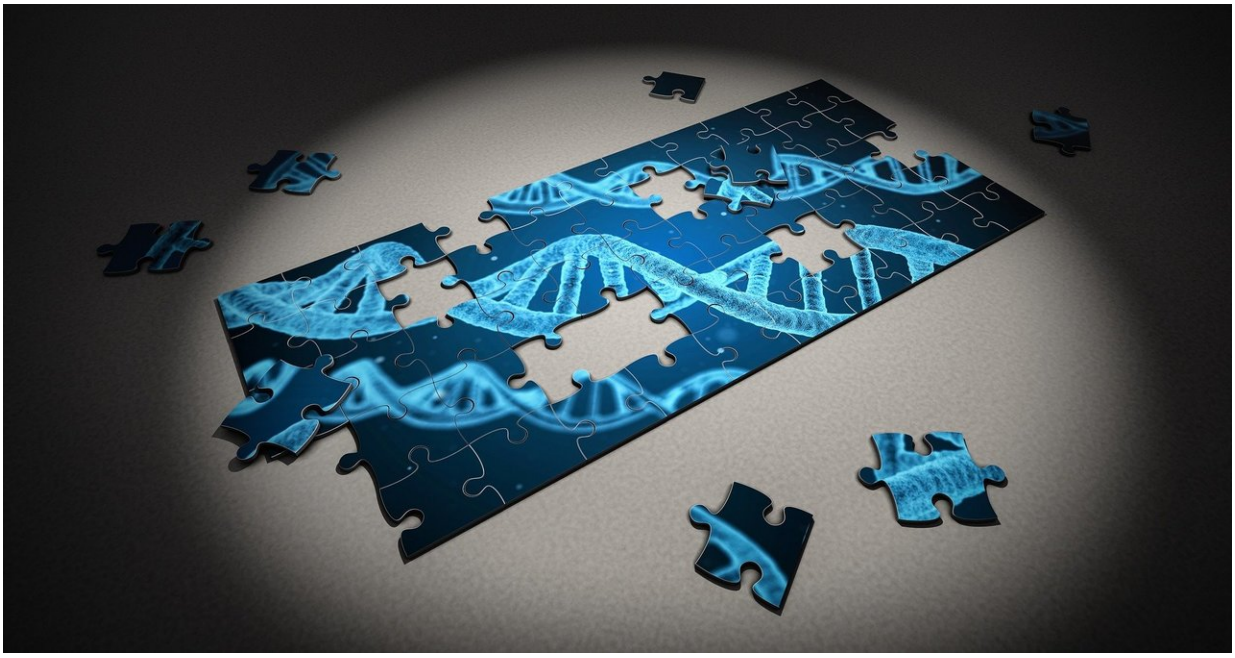

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The transition to modernity, largely driven by the Industrial Revolution, provided us with easier access to food and clean water, with antibiotics, vaccines, and modern medicine. Yet modernity did not just bring fewer infectious diseases and longer life: it also created an environment radically different from the one we evolved in. Genes helpful in our evolutionary past may now predispose us to chronic diseases such as

cardiovascular diseases and cancer in old age. In a paper published in the journal *Nature Reviews Genetics*, an international team of five scientists collate the evidence for this mismatch between past evolutionary adaptation and our modern lives. They also ask whether natural selection linked to modernization might reduce globally the burden of some chronic diseases.

Over the last four centuries, human ecology, life styles and life histories have dramatically changed. The transition to modernity also altered the major causes of human death. Infectious diseases prevalent in childhood have given way to chronic diseases associated with aging. Naturally, as everyone dies, if some causes of death decrease, others must increase in proportion. However, the increasing differences between the circumstances our genes have adapted to and our new environment also plays an important role.

Aging is, in part, caused by the combined effect of many genes that are beneficial when young, but have adverse effects at older ages. Genes can influence a variety of traits and can also express themselves differently as we age (pleiotropy). The term antagonistic pleiotropy describes genes that can carry both beneficial and detrimental effects. Somewhat counterintuitively, evolution by natural selection can lead to antagonistic pleiotropy spreading in populations: The benefits received when young can outweigh the evolutionary disadvantages in old age. Some variants of the gene BRCA1 are, for example, beneficial to fertility. However, women who carry one variant of BRCA1 will, more likely than not, develop breast cancer by the age of 90.

"Angelina Jolie's decision to opt for a preventive double mastectomy instead of risking breast cancer was based on her carrying a high-risk BRCA1 variant," says Virpi Lummaa, professor at the University of Turku in Finland. "This gene variant hasn't been eliminated by natural selection in the past, precisely because it also has a great benefit for

female fertility. Nowadays, the situation is much worse. Due to our much lower fertility levels and longer lifespans the early benefits of such genes no longer play out."

"It is clear that some mutations that benefit fertility have been favoured by natural selection despite heavy costs in old age. It seems likely that these genes have contributed to the rise in chronic disease in modern societies, but it's still uncertain if these genes are the main cause of that increase or just a minor contributing factor," says Jacob Moorad, from the University of Edinburgh.

In contrast, the evolutionary impact of contemporary life on human health is difficult to establish: evolutionary change often requires many generations to leave an unambiguous trace in our genome. The review found "suggestive but not yet overwhelming" evidence that natural selection, the engine of evolution, is changing course in our modern times. Several studies in pre- and post-industrial populations point, for example, to a selection toward an extended fertility period in women.

"We have to be cautious here, though," says Stephen Stearns, professor at Yale University in the USA. "Changes in human biology are driven by two non-exclusive processes. The environment directly impacts how our genes are expressed: Bad nutrition in childhood can cause, for example, stunted growth. But the environment also shapes natural selection. Natural selection can make some genes more – and others less – frequent in the population over time: Lactose-intolerance in adults, for example. It's tempting to point to natural selection when we observe a particular change. However, particularly when the changes occurred recently, it is more likely that gene expression has changed, rather than that the genes themselves have adapted to a new environment."

"Future studies and methodological development can help us clarify the extent to which chronic disease and genetic expression are linked and

whether natural selection begins to counteract the increased burden of chronic disease. It is absolutely essential to establishlarge multigenerational cohort studies to create clear evidence", explains Stephen Corbett,Director of the Centre for Population Health at the Western Sydney Local Health District in Australia.

Alexandre Courtiol, scientist at the Leibniz Institute for Zoo and Wildlife Research (IZW) in Berlin Germany, and co-author of this study adds: "Yes, genes are guilty but waiting for natural selection to adapt our great-great-great-grandchildren to our modern environment is inefficient. It may also not work since the modern environment changes at very high pace. The more rational response to the increase in chronic disease is to change our social environment and our lifestyles in ways that better suit us. We all know the recipe: sleep more, eat less junk, be regularly active and pollute less. True, this is difficult to implement but hopefully not impossible."

**More information:** Stephen Corbett et al. The transition to modernity and chronic disease: mismatch and natural selection, *Nature Reviews Genetics* (2018). DOI: 10.1038/s41576-018-0012-3

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